(12) EUROPEAN PATENT APPLICATION

(54) **Tissue oxygen measuring system.**

(57) A tissue oxygen measuring system enabling the automatic and continuous measurement of diagnosing items including cerebral blood flow, cerebral blood volume, and response of cerebral blood volume to arterial carbon dioxide tension uses an oxygen measuring system (1) based on near infrared spectroscopy, a pulse oximeter (2), and an arterial carbon dioxide tension measuring unit (8). A gas blending unit (4) is employed before a ventilator (3) or face mask to control the ventilator so that a rate of a quantity of oxygen and/or a quantity of carbon dioxide to be blended in the air is changed at predetermined intervals. Trigger signals are produced in synchronism with the changes of the gaseous contents of the air, and parameters for computing information regarding the diagnosing items are measured in response to the trigger signals. With repetitive measurements of the parameters, the signal-to-noise ratio can be improved by averaging the data and erroneous data can easily be identified.
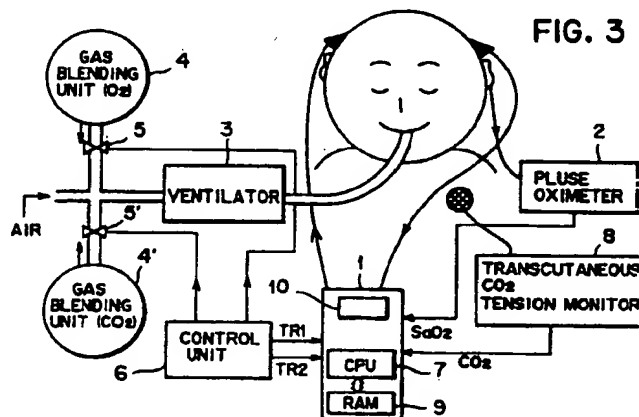
FIG. 3

EP 0 502 270 A1

$$Q = F \cdot \int_0^t \Delta SaO_2 dt \qquad\qquad (2)$$

$$F = Q \cdot \frac{1}{\int_0^t \Delta SaO_2 dt} \qquad (\mu mol/ml \cdot min) \qquad (3)$$

Each of the items in right side of equation (3) is known, so that CBF can be measured. Measurement of CBF is performed in such a manner that following a period when HbO_2 and SaO_2 are stable, a sudden transient increment of 5 to 10% in SaO_2 is induced by increasing the inspired oxygen concentration for a few breaths. During the measurement, blood pressure and values for transcutaneous carbon dioxide tension ($PaCO_2$) are within normal range.

2. Measurement of Cerebral Blood Volume (CBV)

A method of measuring CBV is disclosed in the publication entitled "J. Appl. Physiol.68(3)", pp. 1086–1091.
CBV can be defined by the sum of oxy- and deoxyhemoglobin concentration. Therefore, the following equation is established.

$$CBV = Hb + HbO_2 \qquad (4)$$

As mentioned above, the arterial saturation (SaO_2) can be given from the results of the measurements by means of the pulse oximeter.

$$SaO_2 = \frac{HbO_2}{HbO_2 + Hb} \qquad (5)$$

Because it is assumed that CBV does not change during the maneuver, the changes in [HbO_2] and [Hb] must be equal and opposite. Hence, from the above two equations, the following equation results.

$$CBV = \frac{\Delta HbO_2}{\Delta SaO_2} = \frac{-\Delta Hb}{\Delta SaO_2} = \frac{\Delta (HbO_2 - Hb)}{2\Delta SaO_2} \qquad (6)$$

(3) Measurement of CO_2 Response

The measurement of the CO_2 response is performed while cyclically changing carbon dioxide levels caused either by the addition of a small percentage of CO_2 to the patients gases or by a small cyclic variation in the rate of ventilation. The cycles are at a lower frequency, one every 2 to 10 minutes, since the technique relies on an equilibrium being maintained between the saturations in all blood vessels in the organ.
As described above, the measurement of CBF relies on inducing a rapid change in the patients arterial haemoglobin saturation and then the rate of increase in oxyhemoglobin concentration is observed via the NIR oxygen measuring system. The change in arterial saturation is made by manually and rapidly altering the concentration of oxygen the patient is breathing. Specifically, the quantity of oxygen supplied to the patient from a ventilator is generally changed during 2 to 3 seconds. On the other hand, to measure CBV, the quantity of oxygen is smoothly changed over several minutes. To measure the response of CBV, the amount of carbon dioxide to be blended in the air is also smoothly changed over several minutes. Those procedures have also been done manually and the measurements of those three parameters have been performed individually.

an equal predetermined period of time. The arterial saturation (SaO_2) and the change in the quantity of oxyhemoglobin (ΔHbO_2) in the patient's brain are repeatedly and continuously measured by the pulse oximeter 2 and the NIR oxygen measuring apparatus 1, respectively, during a transit period of time t_1 ranging from 1 to 10 seconds at which the concentration of oxygen is abruptly changed.

The NIR oxygen measuring apparatus 1 incorporates a central processing unit (CPU) 7 therein which is supplied with trigger signals from the control unit 6A. The trigger signals are issued from the control unit 6 in synchronism with the control of the valve 5. In response to the trigger signal, the CPU 7 fetches data from both the NIR oxygen measuring apparatus 1 and the pulse oximeter 2. Data regarding the change in oxyhemoglobin concentration [HbO_2] is supplied from the NIR oxygen measuring apparatus 1, which data is represented by Q in equation (3) and is obtained as a difference b (see Fig. 4A) in the level of the oxyhemoglobin concentrations at the start and end of time t_1. Further, data regarding the arterial oxygen saturation (SaO_2) during time t_1 is supplied from the pulse oximeter 2, which data corresponds to an area indicated by oblique lines in Fig. 4A and denoted by letter a. Those data supplied from both the NIR oxygen measuring apparatus 1 and the pulse oximeter 2 are temporarily stored in random access memory (RAM) 9 connected via a bus to the CPU 7. Based on those data, the CPU 7 performs arithmetic operations in accordance with equation (3) upon reading the data out of the RAM 9. The results of the computation by the CPU 7 is digitally displayed on a display 10 of the apparatus 1. In this manner, a plurality of CBF data are obtained through the repetitive measurements and computations and are collectively displayed on the display 10.

Computation of CBV is performed in accordance with the sequence indicated in Fig. 4B. Specifically, after expiration of time t_2 from the occurrence of the trigger signal in the oxygen-increased cycle, the CPU 7 fetches data A regarding the arterial saturation (SaO_2) from the pulse oximeter 2 and data B regarding the concentration of oxyhemoglobin from the NIR oxygen measuring apparatus 1, and temporarily stores those data in the RAM 9. Then, after expiration of time t_2 from the subsequent trigger signal occurring at the start of the next oxygen-reduced cycle, the same kinds of data A' and B' are fetched and stored in different storage locations of the RAM 9. Then, using the data stored in the RAM 9, the CPU 7 performs arithmetic operation in accordance with the equation of CBV = (ΔHbO_2)/(ΔSaO_2) mentioned previously. That is, CBV is obtained through the computation of (B - B')/(A - A'). Upon completion of the computation, the CPU 7 displays the resultant data in the display 10.

A similar sequence can be employed for the automated measurement of the CO_2, with the use of a small but cyclic change in carbon dioxide levels. The arrangement shown in Fig. 2 is used for such a measurement, which includes the NIR oxygen measuring apparatus 1, a transcutaneous carbon dioxide (CO_2) tension monitor 8, a gas blending unit 4', and a control unit 6B for controlling a valve 5' of the gas blending unit 4'. The monitor 8 has a sensor 11 for attachment to the patient's skin to measure arterial carbon dioxide tension ($PaCo_2$) which tension will hereinafter referred to as "CO_2 tension". The control unit 6B in the arrangement of Fig. 2 controls the valve 5, of a gas blending unit 4' which in this case introduces carbon dioxide into the ventilator 3.

The sequence for measurement of the CO_2 response is illustrated in Fig. 4C. After expiration of time t_2 from the occurrence of the trigger signal at the start of the carbon-dioxide-increase cycle, the CPU 7 fetches data C regarding the CO_2 tension from the monitor 8, and data D regarding a total quantity of the changes in oxy- and dioxyhemoglobin (ΔHbO_2 + ΔHb) from the NIR oxygen measuring apparatus 1. Those data are temporarily stored in the RAM 9. In the subsequent carbon-dioxide-reduced cycle, the same kinds of data C' and D' are similarly fetched and stored. Then, the CPU 7 performs arithmetic operation to provide a ratio of the change in (ΔHbO_2 + ΔHb) to a change of the arterial carbon dioxide tensions attendant to the change of the quantity of CO_2. That is, the CPU 7 performs computation of (D - D')/(C - C'). By repeatedly carrying out the above measurements and computations, a plurality of the CO_2 response data are obtained successively.

As shown in Fig. 4D, both the CBF and CBV can be continuously measured with the arrangement shown in Fig. 1 in accordance with the combined sequence for CBF and CBV.

The control unit 6A periodically changes the oxygen concentration contained in the air supplied to the patient as described previously. During a transit time t_1 in the oxygen-increased cycle, data regarding SaO_2 and ΔHbO_2 measured, respectively, by the pulse oximeter 2 and the NIR oxygen measuring apparatus 1 are fetched and stored in the RAM 9, whereupon CBF is computed and displayed.

After expiration of time t_2 from the occurrence of the trigger signal in the same oxygen-increased cycle, data A regarding the arterial saturation (SaO_2) and data B regarding the concentration of oxyhemoglobin measured, respectively, by the pulse oximeter 1 and the NIR oxygen measuring apparatus 1 are fetched and stored in the relevant storage locations of the RAM 9. Then, after expiration of time t_2 from the subsequent trigger signal occurring at the start of the next oxygen-reduced cycle, the same kinds of data A'

arithmetic operation based on the data fetched in steps S19 and S26 and provides data regarding CO_2 response for displaying the latter in the display 10.

Through the steps S12 through S27, measurements of the three items in one cycle have been completed. In step S28, it is determined whether time 8t has been expired, and if yes, the timer is reset in step S29, and the count number of the internal counter is incremented by one in step S30. Next, it is determined in step S31 whether the count number is equal to N. If no, the routine returns to step S12, and the measurement in the next cycle is performed, whereas if yes, the CPU 7 executes arithmetic operations to provide average data regarding each of CBF, CBV and CO_2 response based on the results of measurements through N cycles and displays the resultant data in the display in steps S32 through S34, whereupon the routine ends.

The above-described sequence according to the present invention can be implemented in the operating theater or intensive care unit (ICU), linked to the ventilator. Since the signal is repetitive, it is possible to employ signal averaging techniques to improve a signal-to-noise (S/N) ratio and to identify erroneous data. Similarly, because one would be averaging, it should be possible to employ smaller swings in the saturation and still obtain accurate results. A further advantage of the repetitive nature of the readings is that one could obtain information on the time delay between the change detected by the pulse oximeter or the CO_2 monitor and that observed by the NIR oxygen measuring apparatus.

While the present invention has been described with reference to specific embodiments, the addition of a small percentage of CO_2 or the addition of oxygen may be made to be in sinusoidal waveform to smoothly change the contents of air to be supplied to the patient. Further, the ventilator can be triggered by the NIR oxygen measuring apparatus or vice versa.

Claims

1. A tissue oxygen measuring system comprising:
   a ventilator unit (3) for supplying air to a living subject for the living subject to breathe;
   a control unit (6) connected to the ventilator unit (3) for controlling the ventilator unit (3) to cyclically change the gaseous content of the air at a predetermined interval;
   means (6) for producing trigger signals in timed relation to the cyclic changes of the gaseous content of the air;
   measuring means (1,2,8) for measuring oxygen in the tissue of the living subject and supplying data regarding measured results; and,
   a data processing unit (7) responsive to the trigger signals for receiving the data from the measuring means (1,2,8) and based on it cyclically computing information regarding blood flowing in the tissue.

2. A tissue oxygen measuring system according to claim 1, wherein the measuring means comprises a first measuring unit (1) for measuring changes in oxyhemoglobin and dioxyhaemoglobin in blood flowing in the tissue by near infrared ray spectroscopy, and a second measuring unit (2) for measuring a saturation of oxygen in an artery.

3. A tissue oxygen measuring system according to claim 1 or 2, wherein the data processing unit (7) cyclically computes at least one of a cerebral blood flow and a cerebral blood volume based on the data received from the first (1) and second (7) measuring units.

4. A tissue oxygen measuring system according to claim 2 or 3, further comprising second measuring means (8) for measuring an arterial carbon dioxide tension of the living subject and providing data regarding measured results.

5. A tissue oxygen measuring system according to claim 4, wherein the data processing unit (7) cyclically computes a ratio of change in cerebral blood volume to change in arterial carbon dioxide tension.

6. A tissue oxygen measuring system according to claim 5, wherein said data processing unit cyclically computes the cerebral blood flow, the cerebral blood volume, and the ratio of change in cerebral blood volume to change in arterial carbon dioxide tension.

7. A tissue oxygen measuring system according any one of the preceding claims, wherein the control unit (7) controls the ventilator unit (3) cyclically to change a rate of oxygen quantity or carbon dioxide
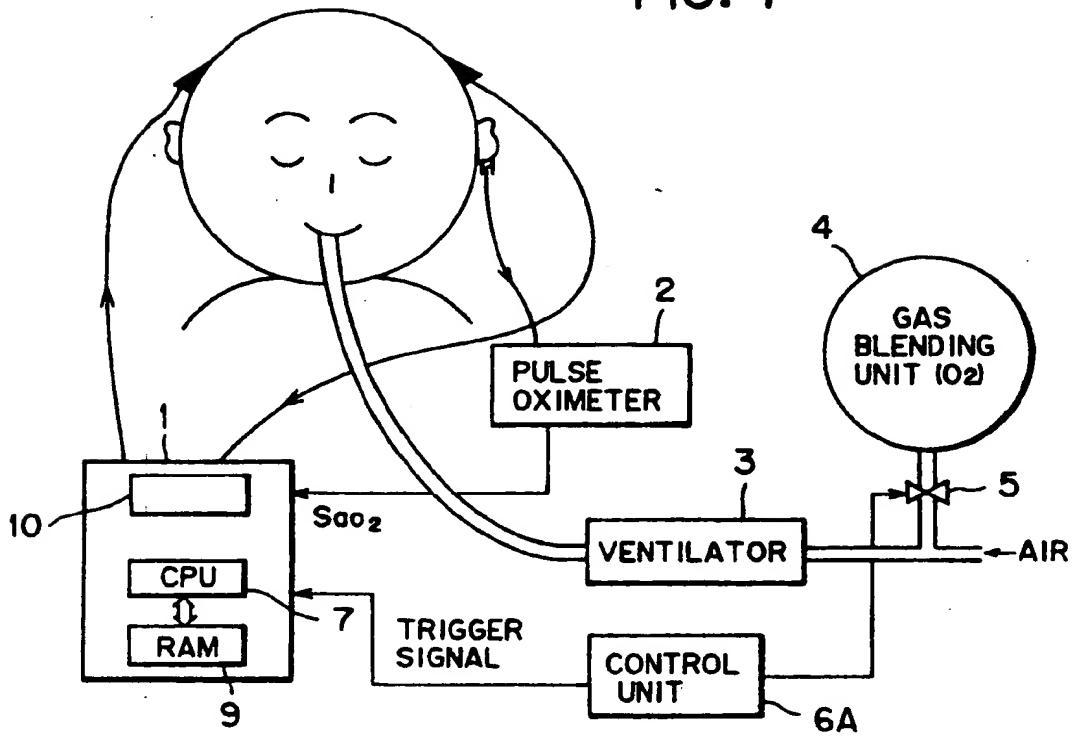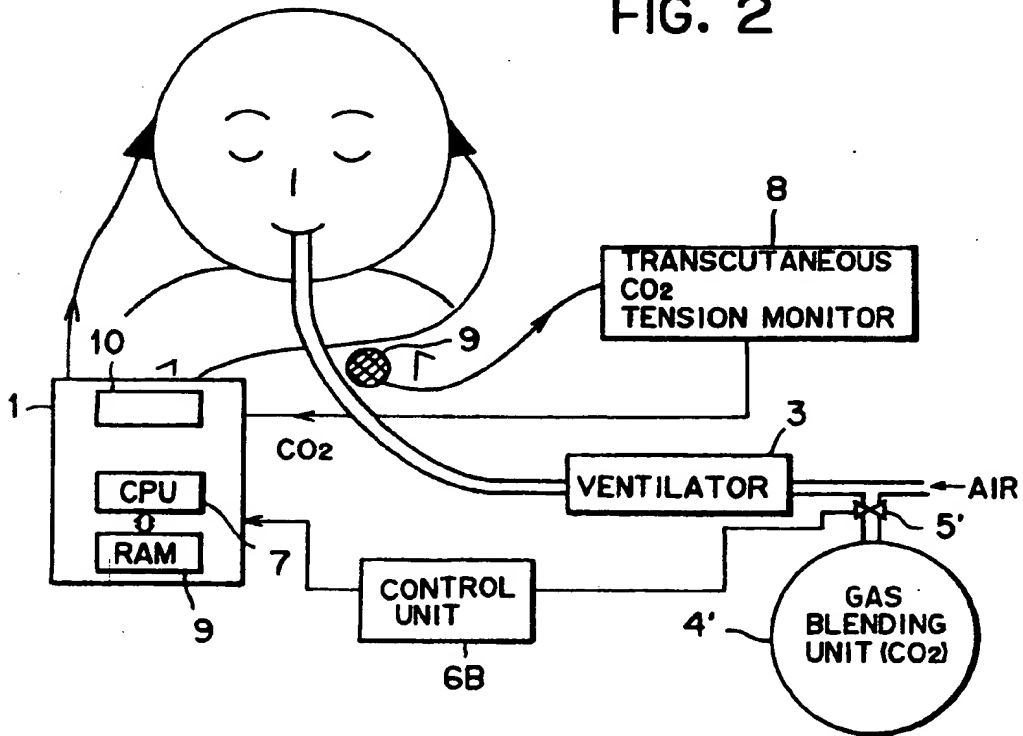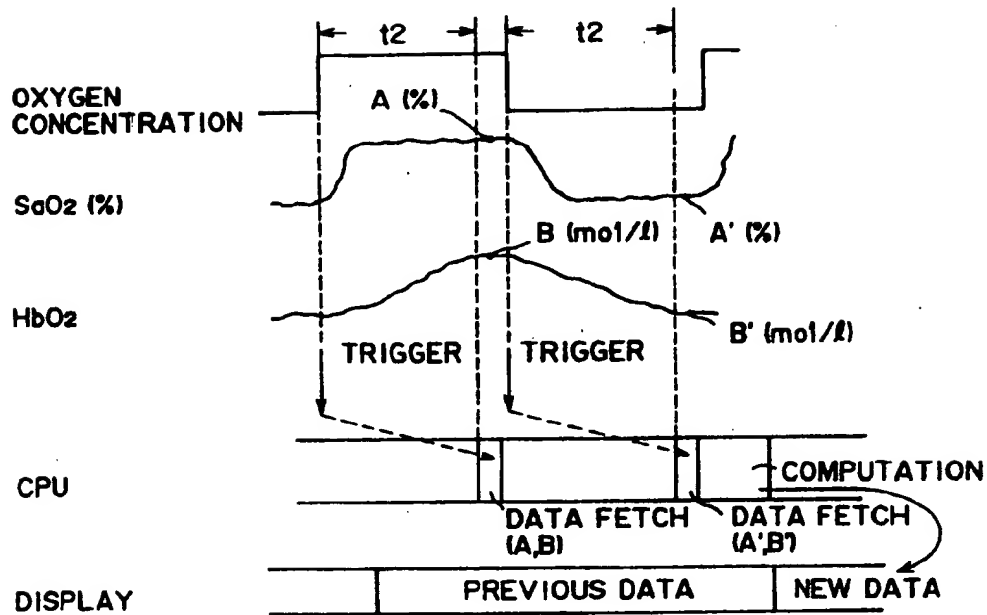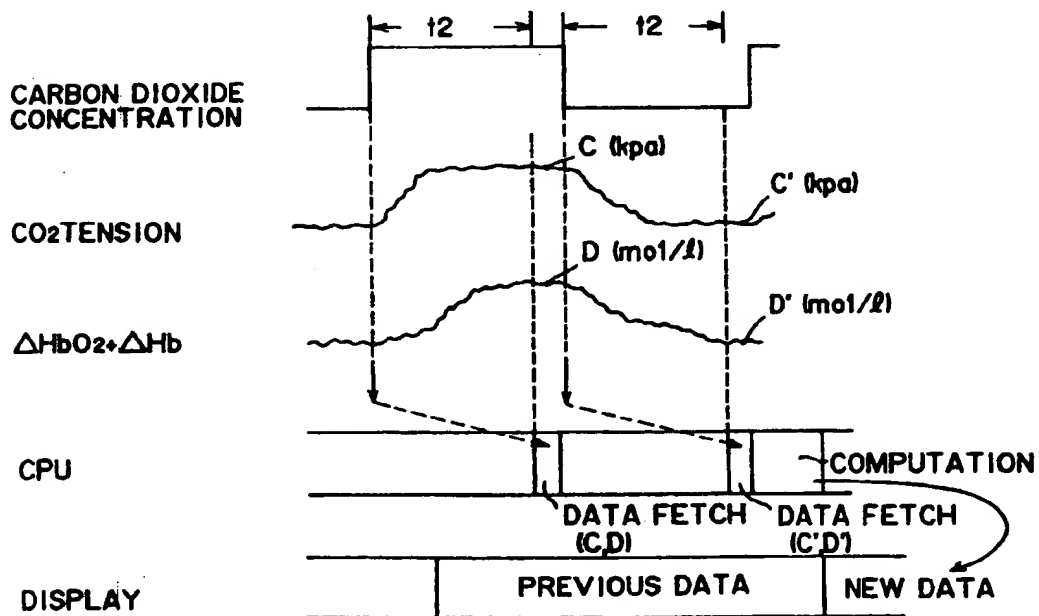
FIG. 1

FIG. 2

FIG. 4B

FIG. 4C

FIG. 5A

START

S1 MEASURE CBF, CBV AND CO₂ RESPONSE ? — NO → S2 MEASURE CBF & CBV ? — YES → S3 FIG. 4D

S2 NO →

S4 MEASURE CBF ? — YES → S5 FIG. 4A

YES (S1) ↓

S10 SET NUMBER OF MEASUREMENT TIMES N

S4 NO →

S6 MEASURE CBV ? — YES → S7 FIG. 4B

S11 PRESET COUNTER

S6 NO →

B

S12 TRIGGER SINGNAL TR2 ? — NO →

S8 MEASURE CO₂ RESPOSE ? — YES → S9 FIG. 4C

YES ↓

S13 SET TIMER

S8 NO →

S14 TRIGGER SINGNAL TR1 ? — NO →

YES ↓

S15 FETCH AND STORE SqO₂

S16 FETCH AND STORE △HbO₂

S17 COMPUTE AND DISPLAY CBF

S18 TIME 2t EXPIRED ? — NO →

YES ↓

S19 FETCH AND STORE (△HbO₂ + △Hb) AND CO₂ TENSION

A

FIG. 5
FIG. 5A
FIG. 5B

EUROPEAN SEARCH REPORT

Application Number

EP   91 30 1920

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	US-A-4 765 340 (T. SAKAI ET AL.) * column 1, line 34 - column 4, line 51 * * column 12, line 3 - line 35; figures 1-3 *	1,7,8	A61B5/00
A	US-A-4 223 680 (F.F. JÖBSIS) * column 5, line 12 - column 9, line 18 *	1-3,6,8	
A	BIOMEDIZINISCHE TECHNIK vol. 35, no. 9, September 1990, BERLIN (DE) pages 185 - 189; S. SCHMIDT ET AL.: 'Laserspektroskopische Erfassung der induzierten Hyperoxie' * page 185 - page 189; figures 1,2 *	1-3,6-8	
A	EP-A-0 267 978 (HELLIGE G.M.B.H.) * column 3, line 39 - column 8, line 1 * * figures 1,2 *	2,4	
A	US-A-4 824 242 (G. FRICK ET AL.) * column 1, line 5 - line 23; figures 6,7 * * column 5, line 51 - column 7, line 36 *	1-3,8,9	TECHNICAL FIELDS SEARCHED (Int. Cl.5) A61B

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	08 NOVEMBER 1991	RIEB K.D.